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Hot topic

Emerging diseases—the monkeypox epidemic in the Democratic Republic of the Congo

Almost 200 years after Edward Jenner's hallmark studies on smallpox immunization and nearly 40 years after the global eradication of the disease by mass vaccination in 1977, the world faces the emergence of another orthopoxvirus infection, monkeypox. The disease was first discovered in 1970 in the Democratic Republic of Congo (DRC). Since then, the majority of cases continue to be reported from the DRC [1–3], yet cases have also been reported from neighbouring Republic of Congo [4] and, in 2006, a cluster from Sudan [5]. In 2003, an outbreak of 47 cases emerged in the Midwestern USA [2,6]. The virus originated from imported West African rodents but then spread further, hosted by and transmitted to humans by prairie dogs [6]. The outbreaks seem to be continuing: in 2013, a substantial rise in the number of monkeypox cases was documented in the DRC [7]; in the Bokungu health zone with 104 suspected cases the increase was over 6-fold compared to previous years [3].

Smallpox virus is the only *Orthopoxvirus* specific to humans. Monkeypox is transmitted within its animal reservoirs and zoonotically, through direct contact between infected animals and humans [1–3,6]. Human-to-human transmission is also possible and household transmission chains as long as seven or more have been reported [3]. The disease closely resembles smallpox: after a mean incubation time of 8 days (4–14 days) [3], most patients first experience fever and headache, and then, a few days later, a characteristic rash appears and the fever subsides [1–3,8]. This rash stage is often accompanied by maxillary, cervical and inguinal lymphadenopathy not typical to smallpox. The rash is usually confined to the trunk but can spread to the palms and soles of the feet, occurring in a centrifugal distribution. The initial macular lesions exhibit a papular, then vesicular and pustular appearance. The most common differential diagnostic disease is caused by varicella zoster virus (chickenpox). Chickenpox develops more rapidly, lesions usually evolve pleomorphically in a centripetal distribution, and are often less severe in presentation [1–3,8]. There are two distinctive clades of the virus, West and Central African; the latter appears to cause a more severe disease and is associated with higher fatality rates. The majority of cases have been diagnosed from Central Africa and only a few from West Africa, the likely origin of the virus in the US outbreak [1,2].

Why is the disease emerging in DRC?

Previous studies suggest that there are several factors contributing to emergence: (a) waning immunity to monkeypox poxviruses in individuals previously vaccinated against smallpox; (b) increasing proportion of individuals born after cessation of vaccination programmes; (c) increased opportunity for human-to-human transmission; and (d) increased exposure to animal reservoir species [1].

The most important factor in the emergence of monkeypox is probably the decreasing immunity to poxviruses in exposed populations. It is attributed both to waning cross-protective immunity among those vaccinated before 1980 when mass smallpox vaccinations were discontinued, and to the gradually increasing proportion of unvaccinated individuals. Smallpox vaccination provides some cross-protective immunity against monkeypox and is most commonly described in unvaccinated individuals [1,2,9]. Active surveillance in DRC in 1980 suggested a cross-protective rate of 85% [1,2,9]. The immunity appears long-lasting: in a study from 2005 to 2007 <4% of patients had a history of prior smallpox vaccination [1]. However, in the US outbreak, 6/11 of infected individuals had received smallpox vaccine in childhood [6].

The increasing proportion of unvaccinated individuals within the community appears to be a major contributor to the problem. In 1980, the proportion of unvaccinated inhabitants was still low in DRC [1,2]. During a surveillance conducted in 1981–86 a total of 338 cases were reported. In a representative region, 35 cases were identified with an estimated incidence of 0.72 cases/10 000 inhabitants. Twenty years later (2006–7), 760 cases were reported in a similar region with an incidence of 14.42 cases/10 000 individuals. These data indicate a 20-fold increase in cases, concomitantly with a decrease in the proportion of vaccinated inhabitants from 84.7% during the first surveillance period to 24.5% during the second. Since then, the proportion of vaccinated individuals has further decreased and the population is therefore even more susceptible.

A remarkable difference between smallpox and monkeypox is that the latter not only infects humans but also has a reservoir in animals. The disease occurs almost exclusively in small remote villages close to the tropical rainforest. Monkeypox virus can infect a large variety of species within the mammalian taxa, ranging from rodents to primates [2]. In particular, squirrels of the *Funisciurus* and *Heliociurus* genera appear to be important reservoirs and likely sources for human disease. Years of war, migration and poverty in the DRC have increased the human penetration into jungle areas and the use of rodents as a food source, potentially increasing the exposure rates substantially.

Recent data suggest that human-to-human transmission has also increased during this time [1,3]. When smallpox vaccinations were first discontinued, only the youngest family members were

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left unvaccinated. Today, entire households are mostly or completely susceptible, allowing significant potential for an additional human-to-human transmission. During the 2013 outbreak in DRC, frequent transmission was documented within households [3,7] with a median attack rate of 50% [7]. A recent study [7] observed that the group most often affected is school-aged boys. Risk factors for transmission included sharing a bed or room and using the same utensils with an infected patient. Increased transmission risk associated with factors involving introduction of virus to the oral mucosa. The researchers concluded that educating locals to limit contact with sick people is an important step in prevention [7].

Monkeypox in DRC is a public health concern of increasing magnitude due to ever greater numbers of people seeking refuge in the rainforest and relying on bush meat as a food source. The situation is further exacerbated by waning population immunity, inadequate living conditions, poverty, poor healthcare infrastructure and low levels of education. The outbreak in the USA [6] demonstrates that spread to areas outside Africa is possible, yet it suggests that infection would not become widespread if it enters regions with modern healthcare systems. Smallpox vaccination (with live vaccinia virus), despite its cross-protective efficacy against monkeypox, is no longer an alternative due to the potential risk for atopic and immunosuppressed individuals in the population [2]. Even with the new-generation vaccines being developed [2], complete eradication of the disease is unlikely because monkeypox has an animal reservoir. The burden of human monkeypox infection in endemic regions may be reduced through a multipronged approach, including (a) health education campaigns addressing handling of potential animal reservoir species to prevent animal-to-human transmission and (b) barrier nursing practices and isolation of acutely infected patients to prevent human-to-human spread. Indeed, the situation calls for increasing awareness and action (adequate decisions, more local medical staff in epidemic regions, adequate sampling, surveillance, education etc.) both from local and international authorities.

Transparency declaration

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Contributions

AK drafted the manuscript; KC, OV, AWR provided critical comments and all authors approved the final version.

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